

CLAIMS

What is claimed is:

- 1 1. A method of making an osteogenic composition, the method comprising:
2 combining purified collagen, an osteoinductive substance, and water containing dilute acid
3 in a dispersing assembly comprising two vessels and a reduced diameter portion, said vessels being
4 in mutual fluid communication by way of said reduced diameter portion;
5 forcing said combination from vessel to vessel through said reduced diameter portion a
6 predetermined number of times sufficient to disperse said collagen and osteoinductive substance in
7 said water, such that said collagen is at least partially hydrated and a dispersion is obtained;
8 allowing said dispersion to stand for a predetermined time interval.
- 1 2. The method of claim 1 wherein said dispersing assembly comprises two syringes, each
2 having a plunger, and said step of passing said combination from vessel to vessel comprises
3 sequentially depressing said plungers a predetermined number of times such that said combination
4 is subjected to physical forces sufficient to disperse said collagen and osteoinductive substance in
5 said water, such that said collagen is at least partially hydrated and a dispersion is obtained.
- 1 3. The method of claim 1 wherein said predetermined number of passes is up to about 250.
- 1 4. The method of claim 1 wherein said step of passing said combination from vessel to vessel
2 comprises:
3 passing said combination from vessel to vessel a first predetermined number of passes;
4 allowing said combination to stand for a first predetermined time interval;

5 passing said combination from vessel to vessel a second predetermined number of passes;
6 and
7 allowing said combination to stand for a second predetermined time interval, such that a
8 dispersion is obtained.

1 5. The method of claim 4 wherein said first predetermined number of passes is about 5-150.

1 6. The method of claim 4 wherein said second predetermined number of passes is about 5-
2 150.

1 7. The method of claim 4 wherein said first time interval is about 30-60 minutes.

1 8. The method of claim 4 wherein said second time interval is at least about 12-72 hours.

1 9. The method of claim 1 wherein said reduced diameter portion comprises a connector and
2 said step of forcing said combination from vessel to vessel through said reduced diameter portion
3 includes passing said combination through said connector.

1 10. The method of claim 1 further comprising extruding said dispersion to provide an
2 extrudate.

1 11. The method of claim 10 further comprising molding said extrudate.

1 12. The method of claim 10 further comprising drying said extrudate to provide a dehydrated
2 osteogenic matrix.

1 13. The method of claim 12 further comprising sterilizing said dehydrated osteogenic matrix.

1 14. The method of claim 13 further comprising rehydrating said dehydrated osteogenic matrix.

1 15. The method of claim 14 further comprising mixing a bulking material with said rehydrated
2 matrix to provide a shapeable osteogenic implant material.

1 16. The method of claim 15 wherein said bulking material is particulate demineralized bone
2 matrix.

1 17. The method of claim 15 further comprising shaping said osteogenic implant material.

1 18. The method of claim 1 wherein said dispersion comprises approximately 1-8% (wt./vol.)
2 collagen.

1 19. The method of claim 1 wherein said collagen is dehydrated fibrous bovine tendon type I
2 collagen.

1 20. The method of claim 1 wherein said water containing dilute acid comprises about 10 mM
2 HCl.

1 21. The method of claim 1 wherein said osteoinductive substance is chosen from the group
2 consisting of bone growth proteins, bone morphogenetic proteins 1-13, osteogenic protein-1 or 2,
3 FGF-I or -II, TGF-beta, GDF-5,6 or 7.

1 22. The method of claim 1 further comprising combining a biologically active agent other than
2 said osteoinductive substance with said collagen/osteoinductive substance, said agent chosen from
3 the group consisting of growth factors, cartilage inducing factors, angiogenic factors, hormones,
4 antibiotics, antiviral compounds and anticancer compounds.

1 23. A method of making an osteogenic composition, the method comprising:
2 combining a predetermined amount of purified collagen, a predetermined amount of an
3 osteoinductive substance, and a predetermined amount of a dilute aqueous acid solution in a
4 dispersing assembly comprising two vessels connected by a reduced diameter portion, said vessels
5 being in mutual fluid communication;

6 passing said combination from vessel to vessel a predetermined number of times such that
7 said combination is subjected to physical forces sufficient to disperse said collagen and
8 osteoinductive substance in said water, such that said collagen is at least partially hydrated and a
9 thickened dispersion is obtained;

10 allowing said thickened dispersion to stand for a second predetermined time interval, such
11 that a thick, extrudable dispersion is obtained;

12 extruding said thick, extrudable dispersion to provide an extrudate; and

13 drying said extrudate to provide a dehydrated osteogenic matrix.

- 1 24. An osteogenic composition comprising a product of the method of claim 1.
- 1 25. The osteogenic composition of claim 24 comprising a mixture of purified type I bovine
2 fibrillar tendon collagen and an osteoinductive substance.
- 1 26. The osteogenic composition of claim 25 further comprising an active agent other than said
2 osteoinductive substance, said agent chosen from the group consisting of growth factors, cartilage
3 inducing factors, angiogenic factors, hormones, antibiotics, antiviral compounds and anticancer
4 compounds.
- 1 27. The osteogenic composition of claim 25 further comprising a bulking material combined
2 with said mixture.
- 1 28. The osteogenic composition of claim 27 wherein said bulking material is particulate
2 demineralized bone matrix.
- 1 29. The osteogenic composition of claim 25 wherein said osteoinductive substance is chosen
2 from the group consisting of bone growth proteins, bone morphogenetic proteins 1-13, osteogenic
3 protein-1 or 2, FGF-I or -II, TGF-beta, GDF-5,6 or 7.
- 1 30. A method of making an implantable osteogenic device comprising:
2 preparing an osteogenic composition according to the method of claim 10;
3 dehydrating said extrudate to yield a dehydrated osteogenic product;

4 rehydrating said dehydrated product;
5 mixing said rehydrated product with a bulking material to provide a shapeable osteogenic
6 implant material.

1 31. The method of claim 30 further comprising shaping said osteogenic implant material to
2 provide an implantable osteogenic device.

1 32. A shaped osteogenic device comprising a product of the method of claim 31.

1 33. A method of making an implantable osteogenic device comprising:
2 preparing an osteogenic composition according to the method of claim 10;
3 dehydrating said extrudate to yield a dehydrated osteogenic product;
4 rehydrating said dehydrated product;
5 inserting said rehydrated product into a spinal cage to provide an osteogenic device.

1 34. An osteogenic spinal cage comprising a product of the method of claim 33.

1 35. A method of inducing osteogenesis in a subject in need thereof comprising implanting in
2 said subject at a site where osteogenesis is desired a device according to claim 30.

1 36. The method of claim 35 wherein said site is a dental or periodontal defect site.

1 37. A method of inducing osteogenesis in a subject in need thereof comprising implanting in
2 said subject in the disk space between two vertebral bodies that are desired to be fused together an
3 osteogenic spinal cage according to claim 34.

1 38. A kit comprising a predetermined quantity of an osteogenic composition according to claim
2 25 and a sterility-maintaining cover.

1 39. The kit of claim 38 further comprising a mixing container.

1 40. The kit of claim 38 further comprising a predetermined quantity of a bulking material.

1 41. A method of making a collagenous matrix comprising:
2 combining collagen and a water containing dilute acid in a dispersing assembly comprising
3 two vessels and a reduced diameter portion, said vessels being in mutual fluid communication by
4 way of said reduced diameter portion;
5 passing said combination from vessel to vessel a predetermined number of times such that
6 said combination is forced through said reduced diameter portion sufficient to disperse said
7 collagen in said water, such that said collagen is at least partially hydrated and a dispersion is
8 obtained;
9 allowing said dispersion to stand for a predetermined time interval to yield an extrudable
10 dispersion.

1 42. The method of claim 41 further comprising molding said extrudable dispersion.

1 43. The method of claim 41 further comprising dehydrating said dispersion.

1 44. The method of claim 43 further comprising rehydrating said dehydrated dispersion.

1 45. The method of claim 44 further comprising mixing a bulking material with said rehydrated
2 dispersion.

1 46. The method of claim 41 further comprising combining a biologically active agent with said
2 collagen and water.

1 47. The method of claim 41 wherein said collagen comprises about 1-8 wt% of said dispersion.

1 48. A collagenous matrix comprising the product of the method of claim 41.

1 49. A method of administering a biologically active agent to a subject in need thereof
2 comprising:

3 preparing a delivery vehicle comprising the collagenous matrix of claim 41;

4 incorporating a biologically active agent into said delivery vehicle; and

5 implanting said delivery vehicle at a selected site in the body of said subject; and

6 allowing said biologically active agent to be released from said delivery vehicle at said site.

1 50. The method of claim 49 wherein said implanting comprises surgical placement of said
2 delivery vehicle.

- 1 51. The method of claim 49 wherein said implanting comprises injecting said delivery vehicle.